Symposium I – Pfizer Satellite Symposium on Epilepsy

Epilepsy Management: Matching Drugs to Patients

S 1

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The last 10 years have witnessed the global introduction into clinical practice of 9 new antiepileptic drugs (AEDs). These, together with the established agents, offer substantial choice to doctors treating patients with epilepsy. Most patients with recent onset seizures will be fully controlled with the first or second AED chosen often at moderate and even modest dosing. Since most patients diagnosed in adolescence or adulthood will require to take prophylactic AED therapy lifelong, it is important also to anticipate unacceptable side-effects and long term sequelae. The substantial choice of AEDs makes it possible to take a most holistic approach to epilepsy management. Consideration should be given to the patient's seizures and/or epilepsy syndrome, age, gender, weight, co-morbidities, psychiatric history, concomitant medication and lifestyle when starting treatment. An alternative AED should be substituted if the first is ineffective or poorly tolerated. If two monotherapies fail or if the first AED produces a substantial improvement, a second drug with multiple mechanisms of action should be added. Attempts at seizure control should be made with two or three AEDs but never more. As more novel AEDs become available, the potential increasingly exists for synergism. A wide range of established and modern AEDs with different mechanisms of action, pharmacokinetics, spectra of efficacy, side-effects and interaction profiles are now available. We should make an effort to choose the best monotherapy and combination regimen for each individual patient. An aggressive approach to early optimization of seizure control may prevent the subsequent development of intractable epilepsy. Nevertheless, there is still a substantial minority of patients who are pharmacoresistant to the current AED armamentarium.

Free Paper Presentations

Re-exploring the Cerebrospinal Fluid (CSF) to Serum Glucose Ratio

F 1

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Background
In interpretation of lumbar puncture (LP) findings, CSF glucose is conventionally expressed as a ratio to the simultaneous level in serum. A low ratio indicates hypoglycorrhachia and pathological conditions.

Method
We retrospectively studied the CSF findings in consecutive LPs performed in our ward over 5 years. Patients with conditions known to cause CSF hypoglycorrhacia, uncertain diagnosis and inadequate laboratory data were excluded. Blood for simultaneous serum glucose level was sampled within one hour of LP. ANOVA, Newman-Keuls multiple comparisons test and linear regression were used for statistical analysis.

Results
170 sets of samples from patients with central demyelination (45), neuropathies (66), headache (26), normal pressure hydrocephalus (11), neurodegenerative diseases (8), and others conditions (14) were studied. CSF glucose was <2.2 mmol/L in only one sample. Mean CSF to serum glucose ratio was 0.61 (range 0.21-1.00). Proportion of samples with ratios of <0.50, 0.50-0.59, 0.60-0.69 and ≥0.70 were 18.8, 27.1, 29.4 and 24.7% for all patients, and 6.8, 27.3, 38.6 and 27.3%, 60.0, 24.0, 8.0 and 8.0%, or 61.5, 30.8, 0.0 and 7.7% for patients with simultaneous serum glucose of < 7.8, 7.8-11.1 or >11.1 mmol/L, respectively. Mean CSF to serum glucose ratios were significantly different between patients with simultaneous serum glucose of <7.8, 7.8-11.1 and >11.1 mmol/L (P <0.0001), but not for different neurological conditions (P = 0.5911). Linear regression showed a significant relation between serum and CSF glucose (r = 0.769, P <0.0001) and inverse correlation between serum glucose and CSF to serum glucose ratio (r = -0.569, P <0.0001, y = 0.8 - 0.03x).

Conclusions
Our study demonstrates the CSF to serum glucose ratio is not constantly related to but varies inversely with the simultaneous serum glucose level. A significant proportion of patients without conditions causing CSF hypoglycorrhachia has a low ratio during hyperglycaemia. The coefficient derived from our linear regression model can be applied for adjustment of such deviations.

Prestroke Cognitive Impairment in Stroke Associated with Small Vessel Disease

F 2

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Objectives
Since in stroke associated with small vessel disease (SSVD), prestroke cognitive decline is associated with post stroke dementia, we studied the frequency, determinants, and outcome of prestroke cognitive impairment in SSVD.

Methods
Over a 6 months period, we administered Informant Questionnaire on Cognitive Decline (IQCODE) to close informants of 78 patients who were consecutively admitted to the acute stroke unit within 1 week of admission because of SSVD. Demographic data, vascular risk factors, apolipoprotein E, neuroimaging features (volume of white matter changes, number of silent small infarcts, cerebral atrophy index [CAI]), and outcome (stroke severity, cognition, Barthel index [BI], instrumental activities of daily living [IADL]) were compared between those with (IQCODE >/= 3.4) and without (IQCODE < 3.4) prestroke cognitive impairment. Regression analysis was performed to find predictors of prestroke cognitive impairment.

Results
Nineteen patients (24.4%) had prestroke cognitive impairment. Multivariate regression revealed that only CAI (OR 1.48, CI 1.17 to 1.86, p<0.001) predicted prestroke cognitive impairment. Patients with prestroke cognitive impairment had greater impairment in cognition and IADL than those without it despite both groups having similar stroke severity and BI.

Conclusion
One quarter of patients with SSVD have prestroke cognitive impairment. Cerebral atrophy is associated with prestroke cognitive impairment. Those with prestroke cognitive impairment have more impaired post stroke cognition and IADL than those without it.

Hong Kong Childhood Stroke Registry (HKCSR) — A Study of 50 Cases (1991-2001)

F 3

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Background
A Hong Kong Childhood Stroke Registry (HKCSR) was established for Chinese children.

Objective
To study the clinical presentation, etiology, risk factors and outcome of Chinese children with stroke.

Materials and Methods
A prospective childhood stroke database was collected during 1991-2001 for children with stroke seen in the University of Hong Kong. Neonatal strokes were excluded.

Results
Fifty children (boys: girls = 28: 22) with mean age of 5.4 years were included. The commonest presenting features were seizures and hemiplegia. There were 36 ischemic and 14 haemorrhagic strokes. For ischemic stroke (36), 18 were due to thrombosis - 11 were vascular origin [moya-moya disease (3), neurofibromatosis (2), fibromuscular dysplasia (1) and post-infectious vasculitis (7)]; 5 were haematological [leukaemia (3); thalassaemia (2)]; and 1 each with severe dehydration and Mitochondrial Encephalopathy Lactic Acidosis Syndrome. Of 15 cases with embolic stroke, all had underlying congenital heart diseases. For 14 cases with haemorrhagic stroke, 2 had arteriovenous malformation, 7 had bleeding tendency [leukaemia (2), aplastic anaemia (2), hemophilia (2) and Wiskott Aldrich Syndrome (1)] and 2 had >1 risk factors (leukaemia and sepsis; congenital heart disease with streptokinase infusion after cardiac catheterization). Six (12%) were idiopathic. None had sinovenous thrombosis.

Outcome
The mean follow-up was 6.6 years (1.8-12.4 years). Nine (18%) died, with 5 having ischemic stroke and 4 with hemorrhagic stroke. 44% had neurological deficit, including mental retardation (11), epilepsy (9) and hemiplegia (14). Five had recurrent stroke. Decreased consciousness (p=0.004), hematological cause (p=0.04) and hemorrhagic transformation of ischaemic stroke (p=0.01) were associated with high mortality. Of the 41 survived, the only significant risk factor for long-term neurological deficit was seizure at initial presentation (p=0.04).

Conclusion
The incidence of childhood stroke from our series is 1.7 per 100,000 children per year. The majority had thrombo-embolic stroke. The majority who survived had neurological sequelae.

Outcome of Children with First Febrile Seizure — A Local Cohort Study of 565 Cases

F 4

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Objective
To investigate the clinical profile and outcome of children admitted for first febrile seizure (FS) in Hong Kong.

Methods
A retrospective study was performed for all children admitted to Queen Mary Hospital with first episode of FS for during a 5 years period (March 1998 - March 2003) was conducted. FS is defined as "an event in a neurologically healthy infant or child aged 6 months to 5 years, associated with fever >38°C but without evidence of intracranial infection or a defined cause and with no history of prior afebrile convulsion" (1). Children with pre-existing developmental delay or underlying neurological disorders were excluded.

Results
Of 1113 children admitted during this period with ICD-9 coding of 780.31 for FS, only 565 children were admitted for the first FS. This First FS database consisted of 565 children (boys : girls = 1.4:1). The mean age of onset was 2.1 +/- 1.1 years. Eighty four percent (474/565) was simple FS and 16% (91/565) was complex FS. Family history of FS and afebrile seizures were present in 17.5% and 2.7% respectively.

The commonest infection is upper respiratory tract infection (75%), followed by gastroenteritis (6.3%), lower respiratory tract infection (4.8%), roseola infantum (3.4%), urinary tract infection (1.4%) and clinical sepsis (1%). The isolated organisms included influenza A (11.8%), adenovirus (4.8%), parainfluenza (4.3%), Respiratory Syncytial Virus (2.7%), influenza B (2.1%) [all from nasopharyngeal aspirate], Rotavirus (1.4%) and salmonella (1.4%) [from stool]. There was no significant difference between age of onset, sex, family history of FS, types of infection or causative organisms with presentation as simple or complex FS.

The mean follow-up period was 2.33 +/- 1.69 years. Altogether 103 children had recurrence of FS - with 72% (74/103) having 1 recurrence, 17.5% (18/103) with 2 and 10.5% (11/103) with more than 2 recurrences. The overall recurrence rate was 12.7% by 1 year, 18.7% by 2 years and 20.5% by 3 years.

Early age of onset [p=0.04; OR = 1.9 (95% C.I. = 1.23-2.95)], family history of FS [p=0.04; OR = 1.8 (95% C.I. = 1.07-3.09)] and complex FS [p=0.005; OR = 1.85 (95% C.I. = 1.02-3.27)] were statistically significant risk factors for recurrence. Only 2 children (0.4%) developed afebrile convulsion during follow-up.

Conclusion
The estimated incidence of first FS in our local children is 0.3%. The overall recurrence rate for FS was 20%. Risk factors of recurrence were similar when compared with Caucasians. Type of infections and causative organisms were not important determining factors for recurrence from our study.

Reference
(1) Consensus Development Panel. Febrile seizures: long term management of children with fever-associated seizures. *Paediatrics* 1980;66:1009-12.

Selective Doral Rhizotomy in Children with Spastic Cerebral Palsy

F 5

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Background
Spasticity in children with cerebral palsy has many adverse effects on patient's normal daily function. Selective dorsal rhizotomy (SDR) is one of the many effective surgical options in managing spasticity. SDR has been performed in Tuen Mun Hospital since 1996. Modifications on patient selection and surgical technique continue to be revised every year. We present our latest 2-year experience in managing spastic cerebral palsy children with SDR.

Method
11 patients have undergone SDR between the period of August 2001 to August 2003. The extend of dorsal root to be excised were affected by pre-operative motor assessment, intra-operative motor and EMG assessment. Range of passive moment, Modified Asthworth Score, Gross Motor Function Measure and Gait pattern were recorded before and after operation. Period of follow up included 3 and 12 months. Data during the follow up period were then compared.